Heroin assisted Treatment in Switzerland– a summary

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The background

During the 1980ties, the HIV epidemic called for a reconsideration of maintenance therapies as a Public Health tool, in order to reduce the number of new infections through contaminated syringes and needles. Throughout Europe, the idea of maintaining heroin addicts on opioids became increasingly acceptable, instead of restricting treatment to 'abstinence-only' approaches. Inevitably, the number of patients who continued heroin injecting while being on methadone, increased as well, and the idea of providing those patients with the 'original drug' invited new experimentation with heroin prescribing. Research projects started 1994 in Switzerland, 1995 in the Netherlands, 2002 in Germany and Spain, 2005 in Canada. The UK started reconsidering the former practice and set up a similarly controlled and psychosocially assisted type of heroin prescribing as in continental Europe. In all these projects, the target population were heroin addicts for whom other treatments had failed previously.

The Swiss initiative was part of a National Drug Policy set up by Federal Government in 1991, as a reaction to an enormous increase in heroin injecting, in blood borne infections of i.v. drug users, in drug related delinquency and highly visible open drug scenes ("needle parks"). This policy officially acknowledged harm reduction measures complementing preventive, therapeutic and repressive approaches to curb the drug problems, and it stimulated innovative efforts and their evaluation on all those domains.

The present state

23 clinics are authorised by the Federal Office of Public Health to practice heroin-assisted treatment, with a total of 1'429 treatment slots. 2 clinics are located in penitentiaries. By end of 2006, 1308 patients were enrolled, which constitutes 8% of all maintenance treatments at national level (BAG 2007). All clinics have to comply with a number of obligations regarding management, indication, safety, reporting, and data collection for monitoring. A detailed handbook describes the obligations and the practice rules (BAG 2000).

After the end of the research project in 1996, the Federal Government decided to continue heroin-assisted treatment as a routine option. New patients could be admitted. Health insurance became obliged to pay for the treatment, except for the ongoing collection of monitoring and research data and for a part of the psychosocial support. Data collection and continued education is paid for by the Federal Office of Public Health, a part of psychosocial support by the communities.

The legal basis for heroin assisted treatment is a parliamentary approved Federal Decree, valid until 2009. A revision of narcotic law, as a permanent legal basis, is under way. Diamorphine is registered as a medication for maintenance treatment of opiate dependence.

Indication criteria are :

- diagnosis of opiate dependence (as defined in ICD-10)
- minimal age of 18
- minimal duration of opiate dependence of 2 years
- at least 2 previous treatments without satisfactory results
- documented social and/or health problems related to opiate dependence.

De facto the average age of admitted patients rose within 12 years from 30 to 39 years.

Heroin-assisted treatment is conceived as a comprehensive, assessment-based therapy covering all individual social and health problems of patients, and it is not time limited (BAG 2000).

The average stay in treatment lasts 3 years. The majority of patients receive injectable heroin, and all injections are made under visual control in the clinics. Take-out of injectables is prohibited. Injectable heroin may be combined with oral Methadone or also with oral heroin (retarded and non-retarded tablets). Such combinations are frequently practiced, as they allow for a reduction of the daily visits at the clinic and thereby to engage in daytime activities (education, day programs, jobs). Patients on stable dosages and in a stabilised psychosocial situation my be allowed take-out of oral medications.

Quality assurance has been an important issue from the beginning. An expert committee received all data on side-effects and unexpected events, and an electronic exchange on problems and experiences how to cope with problems among the clinic teams guarantees a rapid and joint reaction. At present, quality management includes :

- a comprehensive handbook on heroin-assisted treatment
- a monitoring centre for side-effects and unexpected events
- a safety assurance expert group
- continued education for the clinic teams on the basis of observed problems and new research knowledge
- a permanent information exchange among teams via e-mail groups.

Research results

Before starting heroin assisted treatment, a comprehensive review and analysis of all previous attempts at prescribing heroin and morphine was commissioned; it came to the conclusion that a new scientific study was justified (Mino 1990).

A first report on the findings from the study period 1994-96 was published as a volume (Uchtenhagen et al 1999), the economic analysis in a second volume (Gutzwiller & Steffen Eds, 2000). A series of journal articles followed, on the basis of data from the study period, from follow-up studies and from additional research on specific aspects. Also, papers on various topics of heroin assisted treatment were published in 2 volumes (Rihs-Middel et al 1997, SFOPH 2005).

The cohort study included 1'035 out-patients with complete admission data, out of 1'151 admissions (difference due to incomplete data), and 16 in-patients in a prison-based unit. For criminological analysis, police record of 604 patients and criminal registers of 561 patients could be used.

The original design of the project (randomisation to injectable heroin, injectable methadone and injectable morphine) had to be cancelled due to serious side effects of methadone and morphine injections, and was replaced by an overall observational cohort study without control group. Sub-studies included

- a randomised controlled trial of heroin-assisted treatment versus any other treatment while staying on a waiting list for the heroin programme (Perneger et al 1998)
- a double blind randomised trial with cross-over design using injectable heroin versus injectable morphine (Hämmig 1997)
- a randomised trial testing injectable heroin versus injectable methadone and injectable morphine (Ladewig et al 1997)
- a study on injectable methadone (Uehlinger et al 1996)
- pharmacological studies : pharmacodynmics and –kinetics of diacetylmorphine including various application forms (injectable, smokable, inhalable, oral slow-release, suppositories, Brenneisen et al 1997), laboratory tests on diamorphine (Kintz et al 1997)

- toxicology of diacetylmorphine including side-effects (Hämmig 1997, Ladewig et al 1997, Schmied 1997, Uehlinger et al 1996)
- studies on the criminal involvement of patients in heroin-assisted treatment (Rabasa & Killias 1996, Killias et al 1999)
- economic study on costs and cost-benefit of heroin-assisted treatment (Rossier et al, Frei et al, in Gutzwiller & Steffen 2000).

Main substance-related results :

- frequent histaminic-like reactions from intravenous morphine (morphine correctly identified in double-blind study on the basis of side-effects, low acceptance by patients and high drop-out rate (Hämmig 1997)
- frequent local pain at injection site from intravenous methadone, low acceptance by patients and high drop-out rates (Uehlinger et al 1996 Ladewig et al 1997)
- inter-individual differences in the pharmacodynamics and –kinetics of diacetylmorphine, including distribution volume and clearance, in sweat and hair concentrations (independent of dosage); low bio-availability of heroin cigarettes; rush and high effects with oral preparations (slow-release tablets and capsules) and suppositories, although no heroin or its metabolite was found in the bloodstream (Brenneisen et al 1997)
- mean daily dose of heroin was 491.7 mg (from 498'073 days of consumption), stable dose after 6 months at most, slight decrease over 18 months (Uchtenhagen et al 1999).

Main patient-related results (described in Uchtenhagen et al 1999) :

- Retention rates were 89% over 6 months, 69% over 18 months
- Somatic health increased significantly, especially in regard to general health, nutritional status and injection-related skin diseases
- New infections (HIV, Hepatitis) occurred in a few cases mainly during the first months (Steffen et al 2001)
- Pregnancies (n=12) and birth-giving during heroin-assisted treatment went without complications, no indications of developmental defects in the neonates (Geistlich 1996)
- Psychiatric conditions (depressions, anxiety disorders, delusional disorders) improved significantly
- Significant reduction of illicit heroin use (daily use from 81% to 6% after 6 and 18 months), cocaine use (daily use from 29% to3% at 6 months and 2% at 18 months), benzodiazepine use (daily use from 19% to 2% at 6 and 18 months); no reduction of cannabis and alcohol use (self-report and urine controls except for illicit heroin)(Blättler et al 2002)
- Significant improvements in social status (housing situation, employment status, financial situation)
- Significant reduction of contacts with drug users and the drug scene, significant reduction in needle sharing (Steffen et al 2001b)
- Significant reduction of illegal income and criminal activities according to self report (Rabasa & Killias 1996) and police records (Killias et al 1999).

Main service-related results (Uchtenhagen et al 1999) :

- Feasibility : 23 clinics could be established (2 in polyvalent clinics providing also methadone maintenance treatment, 1 located in a penitentiary)
- Acceptance : after initial neighbourhood problems, clinics were well tolerated by security forces and the general population
- Safety : no diversion of prescribed diamorphine to the illegal market, no overdose death from prescribed substances, no major aggressions towards staff

- Staff : competent and dedicated staff could be recruited, organising their own mail groups for rapid exchange of experience.

Main economic results (Rossier-Affolter 2000, Frei et al 2000):

- Lower costs compared to imprisonment, higher costs compared to methadone maintenance treatment (due to higher cost for staffing clinics daily incl. weekends and holidays)
- Calculated daily benefits are almost double compared to daily costs (CHF 95.50 versus 51.17 per patient day).

A *sub-study with randomised design* with an experimental group (n=27) and a waiting-list control group (who received conventional treatment, mostly methadone maintenance, n=21) showed significant differences after 6 months in daily illicit heroin consumption, mental health, social functioning, illegal income and delinquency. There were no benefits in terms of somatic health, housing, work and use of other drugs. Unexpectedly, only 9 control subjects entered the heroin maintenance progamme at follow-up (Perneger et al 1998).

A reduction of delinquency during the first 6 months in treatment could be seen from three data sets. Self-report data from a subgroup of patients entering heroin assisted treatment after April 1, 1995, of which the first follow-up interviews 6 months after entry could be achieved until May 31, 1996, were analysed in regard to involvement in criminal activities (n=248, Rabasa & Killias 1996, Killias & Uchtenhagen 1996). They showed significant reductions in thefts, robbery, burglary and drug trafficking within the first 6 months after entering treatment (all $p<0.0001$). An analysis of police records (n=604) showed also a significant reduction in incidence rates for robbery during the first 6 months after treatment entry (from 1.92 to 0.16, and victimisation rates for robbery during the first 6 months in treatment were reduced from 0.273 to 0.086 (Killias et al 1998).

A special study on the *utilisation* of the heroin clinics and on the characteristics of all admissions and discharges between 1994 and 2001 (n=2'199) came to the following conclusions (Gschwend et al 2003):

- the number enrolled in heroin-assisted treatment increased almost constantly over the years
- 10% of patients entered the treatment more than once
- the average age of new admissions increased from 30 to 35 years, while the rate of female patients decreased from 33 to 25%
- patients remained in heroin-assisted treatment on average for 3.7 years (median 2.8 years)
- 1'233 patients were during these years discharged at least once (24% within the first 4 months, 46% remained between 4 months and 2 years, and 30% longer than 3 years). Early discharges decreased significantly over time.

The *long-term course* has been analysed on the basis of 6-year follow-up data, including the first cohort entering the programme between January 1994 and March 1995 (n=366). 80% were available for personal follow-up interviews, including those patients who had left the programme (54% of those still alive). The mean length of stay in treatment of those remaining in treatment was 6.1 years (SD 0.3 years) since admission, of those who had left the treatment 2.4 years (SD 1.8 years) (Güttinger et al 2003).

Main findings from follow-up studies :

All patients admitted to heroin-assisted treatment between January 1994 and December 2000 (n=2'166 entries, corresponding to1'969 patients) were followed (Rehm et al 2001).

- By December 2000, a total of 1'071 patients was discharged, whereof 90 patients twice and 7 three times
- among the discharged, there was a higher rate of HIV sero-positivity (21% versus 13%)
- retention was found to be relatively high (86% for 3 months, 70% for 12 months, 50% for 2-5 years and 34% for 5 years and longer)
- 59% of discharged patients started another treatment after discharge (22% started drug-free treatment, 37% methadone maintenance)
- the proportion of those switching to drug-free treatment increased with the length of stay in a heroin-assisted programme (29% of discharges after 3 years)
- discharge due to lack of compliance happened in 15% of discharges, mostly during the first months after entering treatment.

The complete cohort entering heroin-assisted treatment between January 1, 1994, and March 31, 1995 (n=366) was followed up for 6 years (Güttinger et al 2003, Gschwend et al 2003).

- 43 patients (11.7%) had died during the 6 years, whereof 5 during their treatment, the rest after leaving treatment
- 148 of the survivors were still in heroin-assisted treatment (n=132 available for interviews), 175 had left treatment without re-entering (n=112 available for interviews)
- the average age was around 36 years in both groups (still in treatment and out of treatment), and in both genders
- the socio-economic status showed a significant reduction since entry to treatment for illegal incomes in both groups, and a significant increase in dependence on welfare and other sources in the treatment group, not in the group out-of-treatment
- daily use of non-prescribed heroin, of cocaine and of benzodiazepines had decreased significantly in both groups; however, the rate of daily illicit heroin use at follow-up was lower in the treatment group than in the out-of-treatment group (3.8% versus 18.9%)
- the rate of integration into the labour market remained unsatisfactory (34% unemployment in both groups), as well as the building up of social contacts outside the drug using community (21.2% and 26.1% respectively have no close friends at all, 24.8% and 18.7% have numerous weekly contacts with currently addicted friends).

An analysis of *mortality* in heroin-assisted treatment over a 7-year period 1994-2000 included all fatalities during treatment and during one month after discharge (n=49) during more than 4'600 person-years. The crude death rate per year varies from 0.0273 (1995) to 0.0063 (2000). The standard mortality rate between 1994 and 2000 is 9.7 (95% CI 7.3-12.8) which is comparatively low. Cause of death, according to death certificates and coded according to ICD-10, included : 34.7% HIV-related, 10.2% other infections, 8.2% cardiovascular diseases, 4.1% cancer, 8.2% other chronic diseases, 18.4% accidents, 16.3% suicide. Prescribed heroin was not causally implicated in any of these deaths (Rehm et al 2005).

Side-effects of prescribed diamorphine were documented routinely in the HeGeBe Monitor, and a special study focused on patients' complaints in a random sample of programme participants (n= 127 out of 1061). The most frequently named immediate symptoms after injection concerned : skin itching (66.9%), profuse sweating (64.2%), reddening of skin at injection site (62.8%); among the less frequent complaints were nausea (29.3%), headache (22.0%), vomiting (18.5%). During the last 7 days, potentially more serious symptoms are memory problems (45.6%), problems with urinating (37.1%), pain in the cardiac region (21.0%), numbness in arms or legs (20.7%), epileptic seizures (5.9%). 5.9% reported

epileptic seizures during the last 12 months. Other factors may have contributes to these symptoms (Dürsteler-McFarland et al 2005).

Two problems became obvious during the years : the high rate of *psychiatric comorbidity*, asking for an improved assessment and care for these patients, and a group unable to reduce their *cocaine use* during heroin-assisted treatment.

Screening of consecutive new admissions to 17 clinics with the SKID (n=85) showed a rate of 86% with a lifetime prevalence of at least one axis-I or axis-II disorder (personality disorders 58%, affective disorders 55%, anxiety disorders 26%, Frei & Rehm 2002a). This demonstrated higher comorbidity rates in comparison to a meta-analysis of 16 studies on the prevalence of co-occurring psychiatric disorders in opiate dependent persons (n=3'754, 78% lifetime prevalence of at least one disorder; personality disorders in 42%, affective disorders in 31% and anxiety disorders in 8%, Frei & Rehm 2002b).

In view of the cocaine problem, a review of the international literature on treatment approaches for cocaine dependence was made available on internet (Stohler et al 2006). Also, a randomised controlled study (Methylphenidate versus placebo, with or without cognitive behavioural therapy in both groups, in addition to regular psychosocial care) was carried out which could not find outcome differences between methylphenidate and placebo, nor between CBT and regular psychosocial care (Dürsteler-McFarland et al 2006).

Studies on *treatment quality* included a detailed comparison of results from the 23 clinics, and also studies on patient satisfaction and quality of life.

The outcome of all new admissions from 1.1.2001 to 29.2.2004 (n=948) were compared in regard to type of treatment termination (favourable versus unwanted). The findings included (Frick et al 2006a):

- treatment centres showed remarkable differences in the ratio of unwanted terminations
- differences are not due to patient characteristics
- an important factor are diverse therapeutic strategies
- overall, the outcomes were similar to those in the original cohort study of 1994-1996; no diminution of positive findings when moving from the original scientific study to routine practice could be observed.

A study on patient satisfaction compared the subjective opinions of patients on injectable heroin with patients on oral heroin (immediate release and slow release tablets), using a list of 42 items on service, staff, therapeutic programme, and on satisfaction with results in the various health, social, substance use domains (all patients on injectable diamorphine of 2003, n=1’200; and all patients on oral diamorphine in 2004-05, n=365). The findings show (Frick et al 2006b) :

- on average a good satisfaction, with the exception of a wish for a more personal care, and dissatisfaction with bureaucracy, job opportunities and sex life
- only marginal differences between application groups, except slightly better satisfaction with the oral preparations
- the satisfaction profile is stable over time (almost identical at entry, at 6 and 12 months).

Changes in key indicators at national level

Since the implementation of the National Drug Policy, we observed not only positive changes in patients enrolled in heroin assisted treatment, but also in regard to some of the main drug related problems in general. This included

- a reduction of overdose mortality by factor 2 since 1991 (Federal Office of Public Health data)
- a reduced incidence of new Aids cases related to i.v. drug use by factor 8 since 1991 (Federal Office of Public Health data)
- a reduced incidence of new heroin users by factor 4 since 1990 (Nordt & Stohler 2006)
- a reduction in heroin related police notifications by factor 2 since 1993 (Federal Office of Police 2005)
- effects of treatment involvement on reducing drug markets (Killias & Aebi 2001).

Heroin has lost it's attractiveness for users of illicit drugs. Qualitative research has demonstrated that heroin is more and more considered to be a "loser drug"; to end up in a heroin clinic has a low image in young people (Von Aarburg & Stauffacher 2005).

In addition, it was advisable to look at the possible consequences of heroin-assisted treatment on the treatment system as a whole. Since 1993, enrolment in methadone maintenance increased by 41%, in drug-free residential treatment by 5%; heroin assisted treatment was not implemented by replacing other therapies, but by complementing it and thereby increasing the estimated treatment coverage for heroin addicts to ca. 70-75%.

These changes are not due to heroin assisted treatment, but it has contributed by reaching out to a most chronic and most damaged and marginalised group of heroin addicts.

International recognition

An international expert group, examining on behalf of World Health Organisation the protocol, implementation and results of the Swiss study, confirmed it's findings, but recommended that further studies should follow a randomisation design in order to determine the value of prescribing Diamorphine in comparison to other substances (Ali et al 1998). This recommendation was the basis for further studies in The Netherlands, Germany, Spain and the UK. Although still being a subject of controversy, there is a growing consensus on the preconditions and conditions of heroin assisted treatment in those countries where it is considered to have a potential role.

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